Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Lyons PA, Rayner TF, Trivedi S, et al. Genetically distinct subsets within ANCA-associated vasculitis. N Engl J Med 2012;367:214-23. DOI: 10.1056/NEJMoa1108735

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SUPPLEMENTARY METHODS

STUDY SUBJECTS

The discovery cohort comprised of 1,233 self-reported UK Caucasian subjects with AAV. The data for 5,884 UK controls were obtained from the Wellcome Trust Case Control Consortium (WTCCC).[1] The replication cohort consisted of 1,454 subjects with AAV recruited from Northern Europe, identified using the same screening protocol as for the discovery cohort. Appropriately matched controls (n = 1,599) were obtained from Germany (n = 467, JUH and SW), the Czech Republic (n = 196, VT and ZH), and the UK Blood Services collection of Common Controls (n = 936).[1] An additional replication cohort comprising 205 cases and 475 controls was obtained from Italy (AV and DM).

The 1992 Chapel Hill Consensus Conference have defined the AAV syndromes, including GPA and MPA, largely according to histological features, but this tool is not suitable for classifying patients in clinical studies. [2] We have chosen the widely accepted EMEA clinically-based algorithm (Table 1 in the Supplementary Appendix and [3]) to classify patients into GPA and MPA for the purpose of this study for the following reasons. 1) A histological system is not practical in a large GWAS study, and cannot be applied on the scale needed for genetic studies. 2) Clinically-based systems are most commonly used in clinical practice. These findings are thus applicable to the “real world”. 3) The great majority of experienced clinicians use ENT disease as a surrogate for GPA, and feel that such disease in MPA patients is uncommon.

The EMEA algorithm was developed for larger scale epidemiologic and genetic studies and is simpler to apply than the EUVAS criteria employed for interventional clinical trials. The latter requires three components: (1) a clinical diagnosis based on a detailed description, largely founded on the CHCC definitions, (2) EITHER ANCA positivity, OR confirmatory biopsy; and (3) absence of an alternative explanation. We formally compared diagnoses from the EMEA algorithm with those from the EUVAS system applied by experienced physicians (DRWJ, ANC, or RAW) blinded to the EMEA-based diagnosis. Results from 250 patients are shown in Supplementary Table 2. The data demonstrate 94% concordance between the methods, with no evidence of consistent differences between them (both MPO and PR3-ANCA patients, and GPA and MPA, move in each direction in the discordant 6%), as expected from published data. [3] Moreover, when we assessed MHC association with GPA and MPA subgroups determined by either method, similar genetic association was observed. Such association was inferior to that found when the 250 patients were divided by PR3- or MPO-ANCA specificity. These observations are supported by a similar comparison performed on an independent cohort of 205 Italian patients (AV).

Both the EMEA and EUVAS classification systems result in classification of patients with ENT disease as GPA. To ensure that genetic associations with GPA were not due to this inclusion of ENT patients, we compared the genetic associations of GPA patients with and without ENT disease. We found that GPA genetic associations are seen in both subgroups, and no statistical difference between them was observed (Table 3 in the Supplementary Appendix)

SELECTION OF SNPS FOR THE REPLICATION ANALYSIS

To select SNPs for replication we imposed a filter of $p<1 \times 10^{-5}$ and a minor allele frequency > 5%, which identified 139 SNPs (Fig. 1B). Imputation (see below) added an additional 1,263. 77 SNPs with prior evidence of association with AAV were included, irrespective of their p value in the primary cohort. Finally 3 SNPs that were not tagged by SNPs on the Affymetrix SNP6 platform were included; *IL2RA* and *PTPN22* because of prior associations, and *PRTN3* because it is a major ANCA autoantigen (*MPO* was represented on the array). From these, 156 non-redundant SNPs were genotyped using the Sequenom MassARRAY platform across a cohort of 1,454 cases and 1,666 controls (1,353 and 1,599 after quality control analyses; Fig. 3B and Table 4 in the Supplementary Appendix).

GENOTYPING

Genotyping of the discovery cohort was performed by AROS Applied Biotechnology (Aarhus, Denmark) using the Affymetrix SNP6 platform which comprises 934,968 SNPs, 612,676 of which passed quality control analysis. SNPs selected for replication were genotyped across the replication cohort using iPLEX assays on the Sequenom MassARRAY platform, both according to the manufacturer's instructions. In addition, four SNPs, rs28929474 and rs17580 (*SERPINA1*), rs5000634 (*HLA-DQ*), and rs62132296 (*PRTN3*) were genotyped using Taqman SNP genotyping assays (Applied Biosystems).

GENOTYPE CALLING AND DATA QUALITY CONTROL

For the discovery cohort SNP genotypes were called from the chip probe intensity measurements using both CRLMM [4] and Birdseed. [5] In both cases, genotype calls with an uncertainty greater than 0.03 were filtered from the output data. Individual samples were removed from subsequent analyses where the Birdseed 'Contrast QC' metric was greater than 0.4, the overall genotype call rate was less than 90%, or heterozygosity fell outside the range 0.27 to 0.36. Duplicated samples or those from closely-related individuals were detected and removed from the study by calculating the fraction of identically-called SNPs between each pair of samples. Subject ethnicity was assessed using Principal Components Analysis (PCA) of the discovery cohort genotype calls combined with genotype calls from HapMap3 populations, [6] and samples falling outside the main Caucasian group according to the first two principal components were discarded (Fig. 3A in the Supplementary Appendix). Sample numbers are shown in Table 4 of the Supplementary Appendix. SNPs were filtered prior to association analysis to remove SNPs where the absolute Z-statistic for the Hardy-Weinberg equilibrium was greater than four, and those for which the call rate was less than 95%. All SNPs chosen for replication had their Affymetrix probe intensity plots visually inspected to confirm correct genotype calling. SNPs in the MHC locus were further selected by applying a lasso penalized regression using MENDEL [7] to identify the best predictor loci within each region.

ASSOCIATION ANALYSIS

Association of SNPs with AAV was determined by applying a standard 1 degree-of-freedom Cochran-Armitage test for additive association implemented in the snpMatrix package [8]. The association analysis was stratified by UK geographic region for the discovery cohort and country of origin for the replication cohort. Odds ratios are shown for the major allele. Stepwise logistic regression was carried out in R. HLA region SNPs which passed our primary cohort significance threshold were used to build a logistic regression model which included the subjects' geographic region as a stratifying variable. A likelihood ratio test (LRT) was calculated to assess the contribution of each SNP to this model, and the least significant SNP discarded. This process was repeated until all remaining SNPs yielded a LRT P-value of less than 1×10^{-3}. This process was conducted separately for the PR3-ANCA and MPO-ANCA cohorts.

Additional SNP genotype calls were imputed from the CRLMM-called genotypes using the HapMap3 reference data (release 27) [6]. Imputation was performed using the snpMatrix Bioconductor package [8]. A second round of imputation was performed against the 1000 genomes pilot study (http://www.1000genomes.org, March 2010), using the MACH software and the snpStats Bioconductor package [9].

Haplotype analysis was performed using the R package “haplo.stats” to calculate maximum likelihood estimates of haplotype probabilities and determine association with disease (version 1.4.4; http://CRAN.R-project.org/package=haplo.stats).

ACKNOWLEDGEMENTS

This study makes use of data for the control subjects generated by the Wellcome Trust Case-Control Consortium. A full list of the investigators who contributed to its generation is available from www.wtccc.org.uk. Funding for the project was provided by the Wellcome Trust under award 076113 and 085475.[1] We acknowledge use of DNA from The UK Blood Services collection of Common Controls (UKBS-CC collection), funded by the Wellcome

Trust grant 084183/Z/07/Z and by NIHR programme grant to NHSBT (RP-PG-0310-1002). The collection was established as part of the Wellcome Trust Case Control Consortium [1]. We thank the U.K. DNA Banking Network for sample storage and preparation during the discovery phase of the study, and AROS Applied Biotechnology (Aarhus, Denmark) and the Wellcome Trust Sanger Institute (Hinxton, UK) for genotyping.

We thank the following for contributing DNA samples and clinical details to this study: CGM Kallenberg and Bram A. Rutgers (Groningen); Jane Hollis (Cambridge); Alan Jardine (KRUK collection); Dr Julie Williams and the Wellcome Trust Clinical Research facility (Birmingham); Professor Raashid Luqmani, Nuffield Orthopaedic Centre, Oxford; Professor Bhaskar Das Gupta, Southend University Hospital, Southend; Professor David GI Scott, Norfolk and Norwich University Hospital; Dr Jaqui Andrews and Dr Richard Baker, Leeds; Dr Mohammed Akil, Royal Hallamshire Hospital, Sheffield, Dr Peter Lanyon, Queen’s Medical Centre, Nottingham; Dr David Carruthers, Birmingham; Dr Katie Vinen, King’s College London; Professor Kuntal Chakravarty, Queen’s Hospital, Romford (Watts Cohort). We thank the Programme Hospitalier de Recherche Clinique (Paris) for support. Finally, we thank the research nurses and patients who contributed to the study.

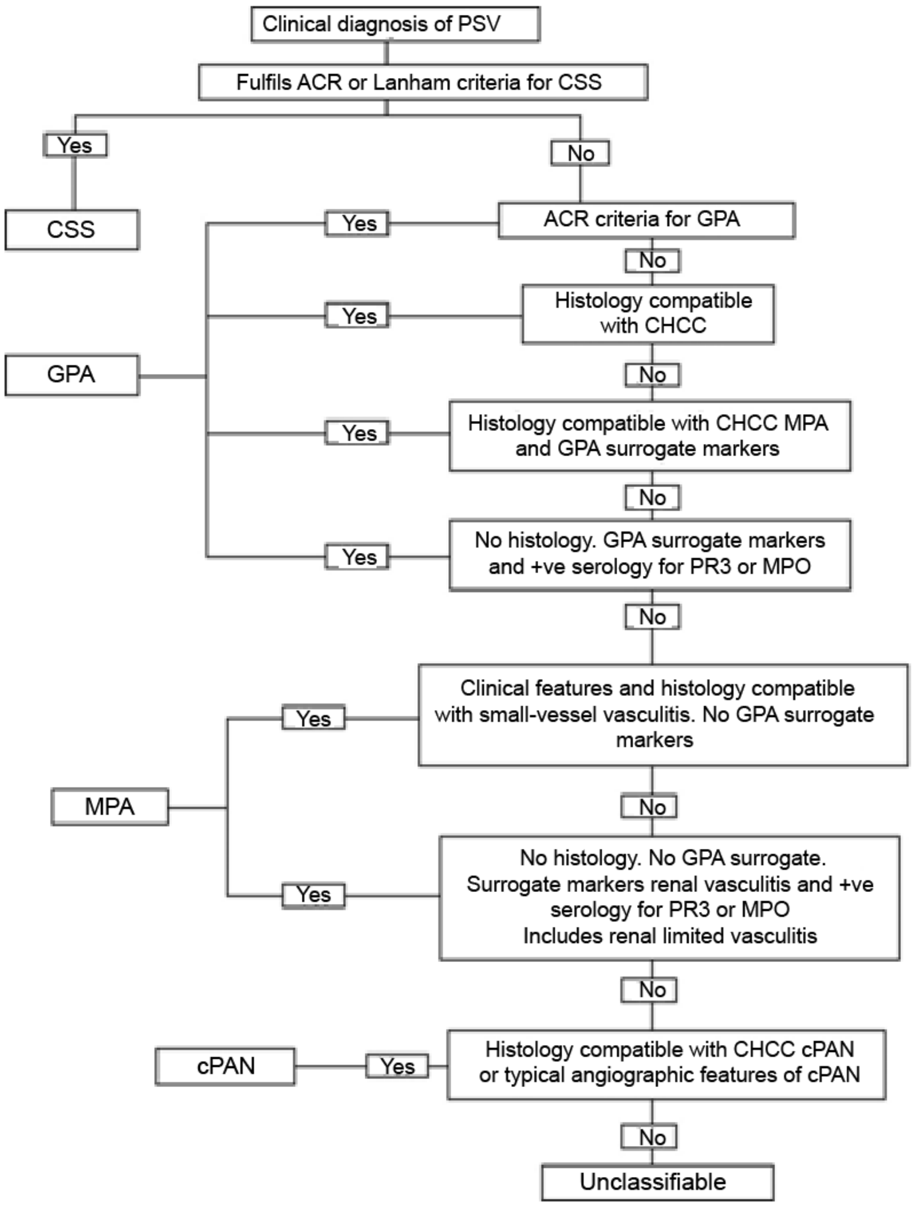


Figure S1. European Medicines Agency (EMEA) vasculitis classification algorithm (adapted from [3]).

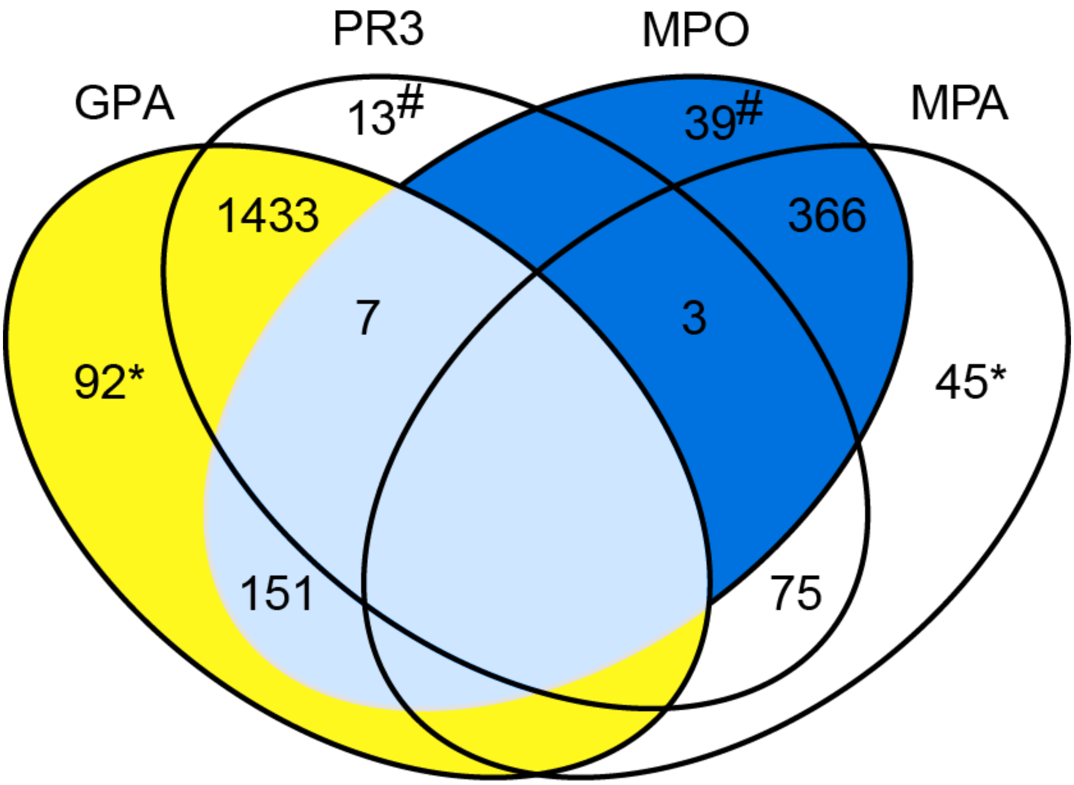
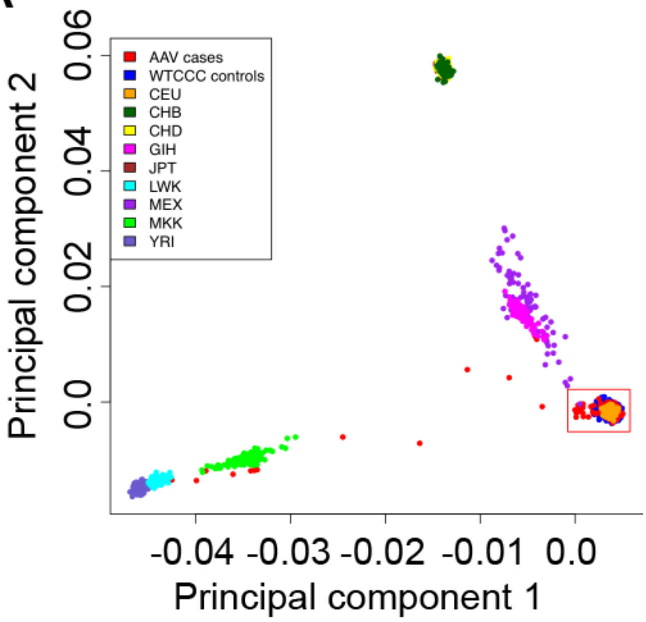


Figure S2. Venn diagram showing relationship between clinical diagnosis and ANCA status in the combined patient dataset. # indicates patients with a clinical diagnosis of AAV and a positive ELISA for either PR3-ANCA or MPO-ANCA but not able to be assigned to either the GPA or MPA subsets. * indicates patients with a clinical diagnosis of GPA or MPA that were C-ANCA or P-ANCA positive by immunofluorescence but for whom no ELISA result was available.

A



B

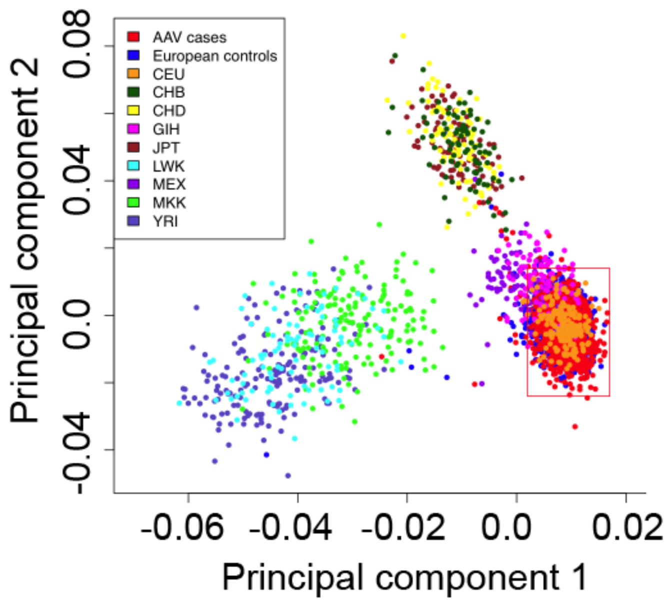


Figure S3. Principal component analysis of primary and replication cohorts.
(A) Principal component analysis (PCA) of genotype data for the cases and controls in the primary cohort together with HapMap individuals was used to exclude samples of non-Caucasian ancestry (those outside the Box). The legend details the ethnic origin of samples included in the PCA; AAV cases, UK cases genotyped in this study; WTCCC controls, UK control samples used in this study; CEU, Centre d'Etude du Polymorphisme Humain (CEPH) individuals collected in Utah, USA; CHB, Han Chinese in Beijing, China; CHD, Chinese in Denver, USA; GIH, Gujarati Indians in Houston, USA; JPT, Japanese in Tokyo, Japan; LWK, Luhya in Webuye, Kenya; MEX, Mexican ancestry in Los Angeles, USA; MKK, Maasai in Kinyawa, Kenya; and YRI, Yoruba in Ibadan, Nigeria. (B) Principal component analysis of the replication case and control cohorts. Legend as for panel A except for the following populations, AAV cases, European cases genotyped in this study, European controls, European controls genotyped in this study. Subjects outside the boxes shown were excluded from further analysis.

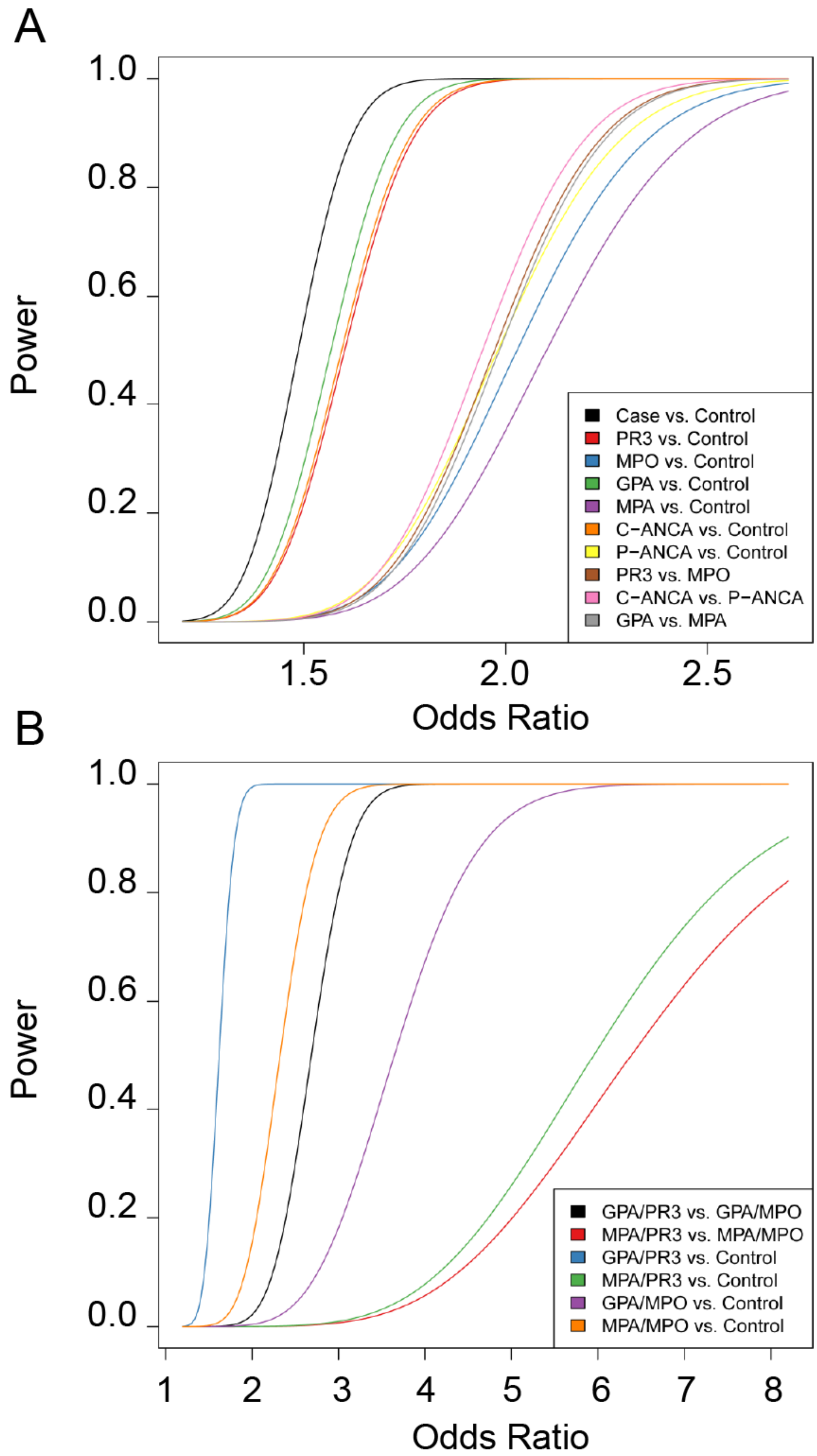


Figure S4. Power curves for the combined and individual subset analyses. Power curves are shown for the combined AAV, GPA v MPA, cANCA v pANCA, and PR3 v MP0 subset analyses (A), and the GPA v MPA analyses subdivided by ANCA status (B). Power was calculated for the various effect sizes assuming a minor allele frequency of 5% and an alpha value of $5x10^{-8}$

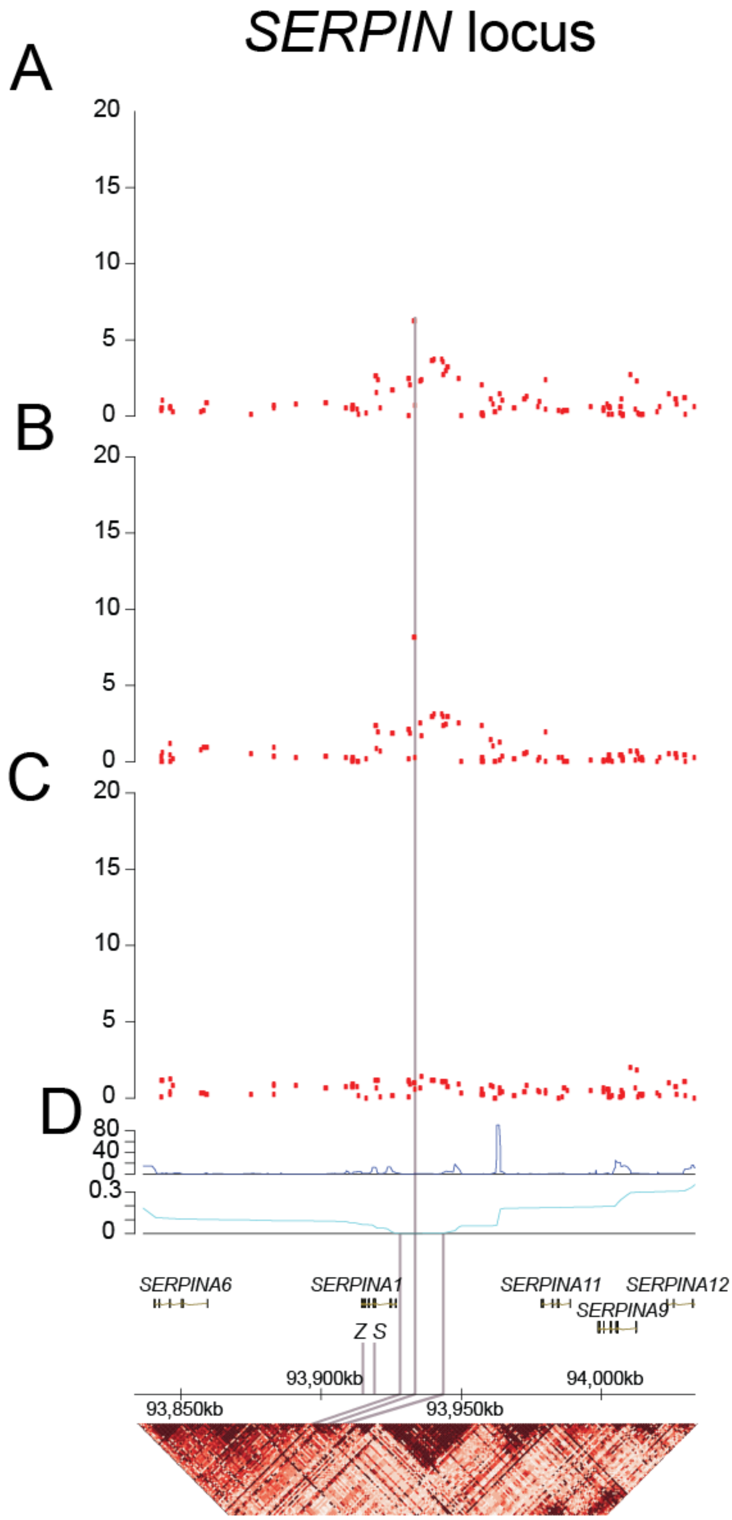


Figure S5. The *SERPINA1* locus shows differential associations with anti-PR3 and anti-MPO positive patients. (A-D) -Log10 p values showing the association of SNPs at the *SERPIN* locus with all AAV cases (A), with anti-PR3 positive cases only (B), and with anti-MPO positive cases only (C). (D) The genomic architecture of the *SERPIN* locus, panels indicate (top to bottom) recombination rate (cM per Mb), cumulative genetic distance from the most associated SNP, gene content of the interval, and haplotype block structure. The grey lines indicate the genomic location of the most associated SNP together with the SNPs defining the Z and S alleles of *SERPINA1*.

Table S1. Inclusion criteria	
Criteria	Response
1. Diagnosis of ANCA-associated vasculitis (excluding Churg-Strauss syndrome)	GPA or MPA
2. Ethnicity: White Caucasian	Yes / No (must be yes)
3. Positive ANCA ELISA (anti-PR3 or anti-MPO)	PR3: MPO:
4. Diagnostic tissue biopsy (with C-ANCA or P-ANCA)	Result:

Inclusion Criteria required a positive response to 1 and 2 & either 3 or 4

Table S2. EMEA and EUVAS physician-based diagnoses are highly concordant, and patients diagnosed with GPA using either approach show similar associations with SNPs within the MHC. Stronger MHC associations are seen with patients positive for anti-PR3 ANCA than with either subgroup of GPA.

	Diagnosis method		ANCA status			
	EMEA	EUVAS	Anti-PR3	Anti-MPO	Both	Total
UK Cohort	GPA	GPA	159	29	3	191
	GPA	MPA	4	5	0	9
	MPA	MPA	12	35	1	48
	MPA	GPA	0	6	0	6
Italian Cohort	GPA	GPA	84	15	1	100
	GPA	MPA	1	1	1	3
	MPA	MPA	2	65	1	68
	MPA	GPA	1	0	0	1

SNP	EMEA GPA v control				EUVAS GPA v control				PR3-ANCA v control			
	UK Cohort n = 200		Italian Cohort n = 115		UK Cohort n = 197		Italian Cohort n =115		UK Cohort n = 175		Italian Cohort n = 86	
	OR	P	OR	P	OR	P	OR	P	OR	P	OR	P
rs3117242	3.0	3.7×10^{-12}	5.23	1.70×10^{-11}	3.0	4.0×10^{-12}	5.23	1.70×10^{-11}	5.8	8.3×10^{-17}	9.79	7.87×10^{-12}
rs3117016	1.7	3.5×10^{-6}	1.90	4.40×10^{-5}	1.8	9.7×10^{-7}	1.94	2.61×10^{-5}	2.3	6.4×10^{-10}	2.47	8.60×10^{-7}
rs3130233	1.5	4.2×10^{-4}	1.30	0.08	1.5	2.9×10^{-4}	1.34	0.05	1.9	3.1×10^{-7}	1.69	1.65×10^{-3}

Table S3. MHC associations in ENT positive and negative GPA patients

		GPA ENT+ve v control (801 v 7,307)		GPA ENT-ve v control (236 v 7,307)		GPA ENT+ve v GPA ENT-ve (801 v 236)	
SNP	Locus	OR	p	OR	p	OR	p
rs3117242	MHC-DP	5.32	1.75×10^{-55}	4.50	4.68×10^{-18}	1.08	0.42
rs5000634	MHC-DQ	0.77	3.94×10^{-6}	0.82	2.60×10^{-1}	0.90	0.64

Table S4. Summary of patient demographics, clinical data and quality control outcomes by cohort

Cohort	Centre	Genotyped	Excluded			Post QC	Clinical breakdown of cases post QC					
			Call rate	Contrast QC	Other		GPA	MPA	PR3-ANCA	MPO-ANCA	c-ANCA	p-ANCA
Discovery	**Cases**											
	Watts DNA bank	465	15	71	28	351	246	81	222	98	226	107
	KRUK DNA bank	359	1	26	17	315	199	81	147	97	186	112
	Birmingham	182	1	10	8	163	71	77	55	50	79	62
	Manchester	157	22	97	3	35	19	7	22	9	20	10
	London	70	2	7	11	50	30	16	35	13	32	16
	Total	**1233**	**41**	**211**	**67**	**914**	**565**	**262**	**481**	**267**	**543**	**307**
	Age at diagnosis (mean ± SD)					55±16	52±16	61±15	53±16	59±15	53±16	59±15
	% male					54%	56%	52%	55%	49%	56%	51%
	Controls	**5884**				**5259**						
Replication	**Cases**											
	Groningen	191	3	0	4	184	143	41	139	42	138	44
	Copenhagen	66	0	0	0	66	64	2	61	5	35	4
	Maastricht	124	0	0	4	120	111	3	88	29	90	29
	Erlangen	116	1	0	3	112	89	23	85	27	85	27
	Bad Bramstedt	429	7	0	12	410	383	27	371	39	370	40
	Lund	96	1	0	3	92	56	36	53	36	49	34
	Karolinska	127	0	0	1	126	96	30	85	38	75	26
	Paris	63	12	0	5	46	46	0	38	4	40	5
	Prague	154	4	0	0	150	87	63	79	64	82	68
	UK	48	39	0	0	9	5	2	4	4	3	4
	Dublin	40	2	0	0	38	38	0	37	1	36	1
	Total	**1454**	**69**	**0**	**32**	**1353**	**1118**	**227**	**1040**	**289**	**1003**	**282**
	Age at diagnosis (mean ± SD)					52±16	51±16	59±15	51±16	60±14	51±16	59±14
	% male					**50%**	53%	41%	55%	34%	55%	35%
Italian	Italy	205			8	197	115	82	86	80	100	97
	Controls	**2141**	**30**	**0**	**63**	**2048**						

Table S5. Ethics approval from each centre

Centre/DNA bank	Ethics number	Ethics committee
Overarching GWAS ethics	10/H0308/1	Cambridgeshire 2 Research Ethics Committee
Watts DNA bank	MREC 03/0/118	MREC for Scotland
KRUK DNA bank	06/MREC05/41	Eastern Multi Centre Reseasrch Ethics Committee
University of Birmingham	O723	Birmingham Local Research Ethics Committee 2
Imperial College London	04/Q0406/25	Hammersmith, Queen Charlotte's and Chelsea ethics committee
Central Manchester University Hospital	06/Q1505/117	North West 2 Research Ethics Committee
University of Groningen	METc2010.057	Medical Ethical Committee at UMCG (University Medical Center Groningen)
Copenhagen University hospital	H-4-2010-125	Region Hovedstaden Ethics Committee
University of Erlangen-Nuremberg	No. 3604	Ethics Committee of the University of Erlangen-Nuremberg
Maastricht University Medical Centre	05-158	Maastricht Local Ethics Committee
Klinikum Bad Bramstedt	AZ 09-185	Ethics Committee of the University of Lübeck
Lund University	Dnr 2010/29	The Regional Ethical Review Board, Lund, Sweden
University Hospital of Parma	29932-08/10/2008	Ethics Committee of Parma University Hospital
Paris	2009-A01331-56	Comite de Protection des Personnes Ile de France X
Karolinska University Hospital	2008/1143-31	Regional Ethics Committee in Stockholm.
University Hospital Prague	1738/07 (S-IV)	Ethics Committee of the General University Hospital in Prague
St James's Hospital, Dublin	01/03/2010	SJH/AMNCH Research Ethics Committee

Table S6. SNPs analysed in the replication phase of the study

								Discovery cohort[a] n = 6173 (914 cases, 5259 controls)			Replication cohort[a] n = 2952 (1353 cases, 1599 controls)			Combined cohort n = 9125 (2267 cases, 6858 controls)	
chr	**position**	**A1**	**A2**	**refsnp**	**gene**	**source**	**z.HWE**	**MAF**	**OR**	***P***	**MAF**	**OR**	***P***	**OR**	***P***
6	33177871	A	G	rs3117242		AAV GWAS	0.83	0.25	2.73	4.09x10^{-36}	0.17	4.29	2.09x10^{-38}	3.67	1.45x10^{-71}
X	5194702	A	G	rs6638512		AAV GWAS	-28.09	0.42	0.48	3.14x10^{-27}	0.49	1.02	9.62x10^{-01}	NA	1.87x10-^{25}
X	119751503	C	T	rs1972809		AAV GWAS	-19.72	0.31	0.43	3.91x10^{-26}	0.4	0.96	4.48x10^{-01}	0.78	1.06x10^{-24}
6	33203494	A	G	rs3117016	COL11A2	AAV GWAS	-2.99	0.38	1.48	3.58x10^{-09}	0.32	2	3.06x10^{-17}	1.83	6.41x10^{-24}
X	88416721	A	C	rs5941160	CPXCR1	AAV GWAS	1.91	0.4	0.51	1.79x10^{-21}	0.34	1.09	2.31x10^{-01}	NA	2.08x10^{-20}
6	33203154	A	G	rs3130233	COL11A2	AAV GWAS	-1.91	0.47	1.33	2.34x10^{-06}	0.44	1.52	8.98x10^{-11}	1.51	7.78x10^{-15}
X	89690783	C	T	rs2755459	TGIF2LX	AAV GWAS	-18.85	0.17	0.46	7.20x10^{-15}	0.24	0.87	3.48x10^{-01}	0.6	8.68x10^{-14}
14	93933389	A	C	rs7151526	SERPINA11;SERPINA1	AAV GWAS	-0.36	0.05	0.56	5.21x10^{-07}	0.06	0.58	1.92x10^{-04}	0.59	2.40x10^{-09}
X	141188237	A	G	rs5954596	MAGEC2	AAV GWAS	-21.12	0.11	0.49	2.50x10^{-10}	0.13	1.01	9.15x10^{-01}	NA	5.31x10^{-09}
X	146850466	C	T	rs5904818	FMR1;FMR1NB	AAV GWAS	-18.4	0.05	0.37	3.28x10^{-09}	0.07	1.13	2.73x10^{-01}	NA	1.96x10^{-08}
X	90699374	A	G	rs6618677	PABPC5;PCDH11X;PCDH11Y	AAV GWAS	2.11	0.14	0.53	2.26x10^{-09}	0.16	0.91	8.34x10^{-01}	0.7	3.98x10^{-08}
X	153886968	C	T	rs17281398	F8	AAV GWAS	-18.7	0.08	0.57	1.38x10^{-07}	0.09	1.28	1.67x10^{-01}	NA	4.30x10^{-07}
6	130073186	A	G	rs17057678	ARHGAP18	AAV GWAS	0.4	0.07	0.63	9.24x10^{-08}	0.06	0.81	3.66x10^{-01}	0.8	6.16x10^{-07}
X	3420669	A	G	rs7059886	MXRA5	AAV GWAS	-18.43	0.23	0.68	2.25x10^{-07}	0.28	0.9	3.36x10^{-01}	0.86	1.31x10^{-06}
13	43953091	A	G	rs17065868	TSC22D1	AAV GWAS	-0.46	0.13	1.48	3.57x10^{-07}	0.13	0.94	4.50x10^{-01}	NA	2.68x10^{-06}

18	3318746	C	T	rs1623523	MRLC2	AAV GWAS	0.3	0.21	1.4	$2.07x10^{-06}$	0.22	1.18	$9.33x10^{-02}$	1.18	$3.18x10^{-06}$
13	29783223	C	T	rs185694	KATNAL1	AAV GWAS	-0.04	0.17	0.69	$1.58x10^{-06}$	0.19	1.06	$1.67x10^{-01}$	NA	$4.26x10^{-06}$
18	53778838	A	G	rs11875185		AAV GWAS	-0.53	0.07	1.64	$4.18x10^{-06}$	0.08	0.81	$1.04x10^{-01}$	NA	$6.83x10^{-06}$
10	36100315	C	T	rs11010290	FZD8	AAV GWAS	-1.52	0.18	0.74	$3.67x10^{-06}$	0.17	1.05	$1.64x10^{-01}$	NA	$9.21x10^{-06}$
17	42304099	C	G	rs11079740	WNT9B	AAV GWAS	0.08	0.11	1.59	$2.08x10^{-06}$	0.11	1.1	$2.90x10^{-01}$	1.1	$9.23x10^{-06}$
X	15090531	A	G	rs6628825	MOSPD2;ASB9	AAV GWAS	-23.16	0.15	0.69	$1.23x10^{-05}$	0.17	0.8	$5.23x10^{-02}$	0.79	$9.78x10^{-06}$
12	94683790	A	G	rs11612530	NTN4	AAV GWAS	-0.67	0.05	0.66	$4.03x10^{-06}$	0.05	0.99	$1.66x10^{-01}$	1	$1.02x10^{-05}$
X	109251916	A	T	rs5985446	TMEM164	AAV GWAS	-21.48	0.13	0.61	$8.13x10^{-07}$	0.17	1.02	$8.79x10^{-01}$	NA	$1.08x10^{-05}$
2	204439764	C	T	rs16840252	CTLA4	AAV GWAS	-0.27	0.17	0.77	$1.11x10^{-05}$	0.17	0.88	$7.67x10^{-02}$	0.87	$1.28x10^{-05}$
X	126856636	C	T	rs766417	ACTRT1	AAV GWAS	-21.51	0.14	0.66	$7.46x10^{-06}$	0.14	1.28	$1.31x10^{-01}$	NA	$1.46x10^{-05}$
4	71056529	A	G	rs17148265	C4orf40	AAV GWAS	-1.61	0.11	1.57	$4.64x10^{-06}$	0.11	1.18	$2.14x10^{-01}$	1.21	$1.47x10^{-05}$
11	88702092	C	T	rs3897708	NOX4	AAV GWAS	1.3	0.14	1.35	$1.15x10^{-06}$	0.17	1.04	$9.23x10^{-01}$	1.05	$1.57x10^{-05}$
8	136490862	A	G	rs2873417	KHDRBS3	AAV GWAS	-0.15	0.07	0.69	$5.61x10^{-06}$	0.06	0.82	$2.69x10^{-01}$	0.82	$2.17x10^{-05}$
13	55561211	C	T	rs166940		AAV GWAS	0.9	0.38	1.23	$2.20x10^{-05}$	0.36	0.89	$7.35x10^{-02}$	NA	$2.32x10^{-05}$
6	89209198	G	T	rs936495	CNR1;RNGTT	AAV GWAS	0.96	0.13	0.78	$4.68x10^{-06}$	0.12	1.14	$3.69x10^{-01}$	NA	$2.46x10^{-05}$
X	23714792	C	T	rs873637	SAT1;APOO;CXorf58	AAV GWAS	-21.79	0.06	0.55	$4.09x10^{-06}$	0.08	1.13	$4.79x10^{-01}$	NA	$2.78x10^{-05}$
X	6144432	A	T	rs16983988	NLGN4X	AAV GWAS	-20.85	0.12	0.73	$4.48x10^{-06}$	0.11	1.11	$4.98x10^{-01}$	NA	$3.13x10^{-05}$
6	150407036	C	G	rs12207804	RAET1L;ULBP3	AAV GWAS	1.26	0.16	1.42	$4.27x10^{-06}$	0.19	0.92	$5.82x10^{-01}$	NA	$3.45x10^{-05}$
11	20838013	A	G	rs1429794	NELL1	AAV GWAS	0.95	0.17	0.8	$5.86x10^{-06}$	0.17	1.02	$4.42x10^{-01}$	NA	$3.59x10^{-05}$
10	26703928	C	T	rs4749119	GAD2;APBB1IP	AAV GWAS	-0.31	0.06	0.66	$6.90x10^{-06}$	0.06	1.13	$4.46x10^{-01}$	NA	$4.21x10^{-05}$
X	121403592	A	G	rs982834		AAV GWAS	-18.77	0.06	0.61	$2.33x10^{-05}$	0.06	1.36	$1.37x10^{-01}$	NA	$4.35x10^{-05}$

22	44116991	A	T	rs2294202	FAM118A;SMC1B	AAV GWAS	0.65	0.11	1.36	$4.62x10^{-06}$	0.1	0.95	$7.19x10^{-01}$	NA	$4.52x10^{-05}$
X	149375434	A	G	rs2266831	MAMLD1	AAV GWAS	-19.9	0.33	0.73	$1.30x10^{-05}$	0.32	1.06	$2.72x10^{-01}$	NA	$4.78x10^{-05}$
1	58224902	A	G	rs4912290	DAB1	AAV GWAS	-1.04	0.08	1.58	$6.49x10^{-06}$	0.09	1.07	$6.65x10^{-01}$	1.06	$5.77x10^{-05}$
8	134316309	A	G	rs13263504	WISP1;NDRG1	AAV GWAS	-0.19	0.33	1.22	$6.41x10^{-06}$	0.34	1.06	$7.10x10^{-01}$	1.07	6.05E-05
9	7199284	A	G	rs7020238	JMJD2C	AAV GWAS	-0.04	0.5	1.23	$8.27x10^{-06}$	0.48	0.96	$6.20x10^{-01}$	NA	$6.76x10^{-05}$
9	13105422	A	C	rs2274647	MPDZ	AAV GWAS	0.34	0.3	1.27	$6.86x10^{-06}$	0.32	1	$8.26x10^{-01}$	1	$7.42x10^{-05}$
5	86929576	C	T	rs984026	TMEM161B	AAV GWAS	-1.45	0.06	0.72	$9.42x10^{-06}$	0.07	0.86	$8.54x10^{-01}$	0.85	$1.02x10^{-04}$
3	193438813	A	G	rs2126071	FGF12	AAV GWAS	-0.01	0.37	0.81	$3.25x10^{-04}$	0.36	1.16	$1.39x10^{-01}$	NA	$4.96x10^{-04}$
12	6040747	A	C	rs12319392	VWF	AAV GWAS	0.91	0.07	0.75	$5.82x10^{-05}$	0.08	0.94	$9.96x10^{-01}$	0.92	$6.23x10^{-04}$
9	100665697	A	T	rs7470086	COL15A1;GALNT12	AAV GWAS	0.01	0.28	0.87	$3.61x10^{-04}$	0.27	1.02	$3.75x10^{-01}$	NA	$1.34x10^{-03}$
8	123532726	C	T	rs10097761	HAS2	AAV GWAS	1.64	0.13	0.85	$3.86x10^{-04}$	0.13	1.03	$3.67x10^{-01}$	NA	$1.40x10^{-03}$
1	114105331	A	C	rs6679677	PTPN22	external candidate	-0.65	0.1	0.78	$6.17x10^{-04}$	0.12	0.8	$2.60x10^{-01}$	0.8	$1.57x10^{-03}$
10	98352911	A	G	rs11188849	PIK3AP1	AAV GWAS	-1.2	0.15	1.24	$7.56x10^{-04}$	0.15	0.9	$5.31x10^{-01}$	NA	$3.54x10^{-03}$
19	34756236	A	G	rs7250581	POP4	external candidate	-0.36	0.21	0.95	$7.71x10^{-01}$	0.2	0.69	$6.12x10^{-04}$	0.72	$4.09x10^{-03}$
12	75658282	C	G	rs10862477	OSBPL8;ZDHHC17	external candidate	-0.35	0.32	1.09	$8.14x10^{-02}$	0.32	0.8	$7.71x10^{-03}$	NA	$5.25x10^{-03}$
18	65678740	A	C	rs1790947	DOK6;CD226	external candidate	1.6	0.48	0.91	1.12x10-01	0.48	0.83	7.68x10-03	0.81	6.95x10-03
16	71567199	C	T	rs10852516	ZFHX3	external candidate	-1.31	0.34	1.04	1.31x10-01	0.36	0.78	6.78x10-03	NA	7.12x10-03
1	65846754	A	G	rs2376018	LEPR	external candidate	0.34	0.17	1.19	1.26x10-02	0.17	1.23	7.08x10-02	1.25	7.15x10-03
16	73063948	C	G	rs8059315	GLG1	external candidate	-0.51	0.19	0.86	4.10x10-02	0.19	1.21	3.01x10-02	NA	9.52x10-03

16	71557266	C	T	rs11075953	ZFHX3	external candidate	-0.46	0.36	1.04	9.07x10-02	0.38	0.82	2.54x10-02	NA	1.63x10-02
19	38822176	A	G	rs2059876	CHST8	AAV GWAS disease subsets	-1.37	0.32	1.17	7.79x10-03	0.32	1.06	4.98x10-01	1.06	2.54x10-02
2	239063597	C	T	rs567962	ASB1	AAV GWAS disease subsets	0.87	0.39	1.02	6.49x10^{-01}	0.42	1.21	1.19x10^{-02}	1.2	4.55x10^{-02}
7	128404702	A	G	rs12531711	TNPO3	external candidate	-1.72	0.11	0.91	3.45x10^{-01}	0.11	0.76	5.04x10^{-02}	0.81	8.80x10^{-02}
18	36256729	C	T	rs16973295		AAV GWAS disease subsets	0.82	0.08	1	9.61x10^{-01}	0.07	1.26	2.35x10^{-02}	NA	1.08x10^{-01}
10	93342936	A	T	rs1329656	HECTD2;PPP1R3C	AAV GWAS disease subsets	-0.88	0.42	1.03	6.99x10^{-01}	0.41	0.9	5.11x10^{-02}	NA	1.55x10^{-01}
12	127580837	C	T	rs7972272	TMEM132C	AAV GWAS disease subsets	0.03	0.31	0.96	1.36x10^{-01}	0.3	1.06	3.49x10^{-01}	NA	1.92x10^{-01}
17	68428059	C	G	rs8069126	SLC39A11	AAV GWAS disease subsets	-0.93	0.31	1.05	2.89x10^{-01}	0.33	0.89	1.68x10^{-01}	NA	1.96x10^{-01}
4	73734689	A	G	rs16848425	ADAMTS3	AAV GWAS disease subsets	-1.96	0.07	0.98	6.85x10^{-01}	0.06	1.27	8.85x10^{-02}	NA	2.30x10^{-01}
20	23554845	A	G	rs12625716	CST9;CST3	external candidate	-0.44	0.23	0.97	6.96x10^{-01}	0.22	1.13	9.25x10^{-02}	NA	2.41x10^{-01}
15	43478281	A	G	rs1346267	SPATA5L1;GATM	external candidate	-0.78	0.37	0.96	7.04x10^{-01}	0.36	1.1	1.07x10^{-01}	NA	2.70x10^{-01}
10	88303616	C	T	rs11202069	WAPAL	AAV GWAS disease subsets	-1.6	0.06	1.24	9.04x10^{-02}	0.06	1.04	9.53x10^{-01}	1	2.97x10^{-01}
6	151294678	A	G	rs6922269	MTHFD1L	external candidate	1.14	0.27	0.96	4.05x10^{-01}	0.27	1.08	3.59x10^{-01}	NA	4.26x10^{-01}

1	238512219	C	T	rs17672135	FMN2	external candidate	0.12	0.13	1	$9.63x10^{-01}$	0.11	0.8	$1.58x10^{-01}$	0.96	$4.39x10^{-01}$
20	9160186	A	C	rs5011374	PLCB4	AAV GWAS disease subsets	-1.53	0.47	0.94	$2.68x10^{-01}$	0.47	1.01	$5.99x10^{-01}$	NA	$4.55x10^{-01}$
1	205010856	A	G	rs1554286	IL10	external candidate	1.44	0.17	0.89	$2.23x10^{-01}$	0.18	1.04	$7.51x10^{-01}$	NA	$4.67x10^{-01}$
2	191407291	A	G	rs16832990	NAB1;GLS	AAV GWAS disease subsets	-0.62	0.23	0.99	$4.43x10^{-01}$	0.24	1.05	$3.85x10^{-01}$	NA	$4.72x10^{-01}$
1	67523062	C	T	rs7546245	IL12RB2	external candidate	1.61	0.32	1.1	$1.84x10^{-01}$	0.28	0.98	$9.28x10^{-01}$	NA	$4.73x10^{-01}$
12	119919970	A	C	rs2259816	HNF1A	external candidate	-0.5	0.35	0.95	$4.28x10^{-01}$	0.36	1.08	$4.13x10^{-01}$	NA	$4.83x10^{-01}$
16	81769899	A	C	rs8055236	CDH13	external candidate	0.71	0.19	1.02	$8.21x10^{-01}$	0.18	0.9	$2.32x10^{-01}$	NA	$5.06x10^{-01}$
11	128302467	A	G	rs1893142	KCNJ5;C11orf45;P53AIP1	AAV GWAS disease subsets	0.19	0.33	1.01	$6.50x10^{-01}$	0.3	0.93	$2.94x10^{-01}$	NA	$5.08x10^{-01}$
1	109622830	G	T	rs583104	PSRC1;CELSR2	external candidate	-1.35	0.23	1.03	$3.10x10^{-01}$	0.24	1	$6.96x10^{-01}$	1.04	$5.46x10^{-01}$
5	85452149	A	T	rs17285524	NBPF22P	AAV GWAS disease subsets	-0.9	0.06	0.91	$2.65x10^{-01}$	0.06	1.11	$8.64x10^{-01}$	NA	$5.67x10^{-01}$
1	220890152	G	T	rs17465637	MIA3	external candidate	-0.02	0.29	0.95	$3.60x10^{-01}$	0.27	1.03	$7.56x10^{-01}$	NA	$6.26x10^{-01}$
2	21202704	A	G	rs312961	APOB	AAV GWAS disease subsets	-0.3	0.37	0.98	$6.80x10^{-01}$	0.38	1.04	$4.60x10^{-01}$	NA	$6.76x10^{-01}$
8	122920781	A	T	rs4268133	HAS2	AAV GWAS disease subsets	-1.47	0.07	0.96	$5.55x10^{-01}$	0.05	1.12	$5.71x10^{-01}$	NA	$6.81x10^{-01}$
3	139604812	C	T	rs9818870	FAM62C;MRAS	external candidate	0.59	0.15	0.96	$3.71x10^{-01}$	0.16	1.01	$8.82x10^{-01}$	NA	$6.93x10^{-01}$

11	111539949	G	T	rs360718	IL18	external candidate	0.49	0.27	0.97	4.86x10^{-01}	0.28	0.97	8.21x10^{-01}	0.94	7.66x10^{-01}
13	77556904	A	T	rs1330882		AAV GWAS disease subsets	0.6	0.18	0.96	8.50x10^{-01}	0.17	1.11	5.03x10^{-01}	NA	7.91x10^{-01}
10	44072982	A	G	rs671765	C10orf136;CXCL12	external candidate	-0.83	0.13	0.95	4.62x10^{-01}	0.14	0.97	9.28x10^{-01}	0.94	7.92x10^{-01}
5	39168604	C	T	rs1125508	FYB	external candidate	-0.56	0.28	1.03	4.70x10^{-01}	0.26	1.01	9.50x10^{-01}	1.02	8.07x10^{-01}
2	226776324	A	C	rs2943634	KIAA1486	external candidate	0.86	0.34	1.02	5.85x10^{-01}	0.34	1.06	7.83x10^{-01}	1.08	8.15x10^{-01}
9	22115503	C	G	rs1333049	MTAP;CDKN2A;CDKN2B;DMRTA1	external candidate	-0.47	0.48	1	5.85x10^{-01}	0.48	1.02	8.88x10^{-01}	NA	8.60x10^{-01}
5	99976881	A	T	rs383830	FAM174A	external candidate	-0.14	0.21	0.99	7.88x10^{-01}	0.21	0.97	8.76x10^{-01}	0.95	9.46x10^{-01}
16	20273155	A	G	rs13333226	PDILT;UMOD	external candidate	-0.18	0.18	1.02	8.91x10^{-01}	0.17	0.99	9.75x10^{-01}	NA	9.91x10^{-01}
19	20464643	G	T	rs10406270	Caucasian SNP	Private Caucasian SNP	-5.08	NA	NA	NA	0.29	1	8.54x10^{-01}	NA	NA
6	160930108	A	G	rs10455872	LPA	external candidate	1.18	NA	NA	NA	0.07	1.05	5.44x10^{-01}	NA	NA
10	73596728	C	T	rs11000199	Caucasian SNP	Private Caucasian SNP	0.05	NA	NA	NA	0	2.33	5.29x10^{-01}	NA	NA
9	70368029	A	G	rs11142941	PIP5K1B;C9orf71;FAM122A	AAV GWAS	0.66	NA	NA	NA	0.45	0.99	9.88x10^{-01}	NA	NA
20	30112373	NA	NA	rs11267532	HCK (indel)	external candidate	1.48	NA	NA	NA	0.31	0.94	2.94x10^{-01}	NA	NA
6	135902107	C	T	rs12203875	AHI1;PDE7B	AAV GWAS	1.05	NA	NA	NA	0.46	0.95	7.83x10^{-02}	NA	NA

1	176231262	C	T	rs1336776	LOC730102;SEC16B	AAV GWAS	0.16	NA	NA	NA	0.18	1.19	1.39×10^{-01}	NA	NA
6	77497656	A	T	rs1545653	HTR1B	AAV GWAS	0.09	NA	NA	NA	0	0.39	6.88×10^{-01}	NA	NA
15	65245693	A	G	rs17228212	SMAD3	external candidate	1.1	NA	NA	NA	0.28	0.97	3.26×10^{-01}	NA	NA
4	77587871	A	G	rs17319721	SHROOM3	external candidate	-0.02	NA	NA	NA	0.45	1.06	4.69×10^{-01}	NA	NA
14	94433903	C	G	rs17754871	DICER1;GSC	AAV GWAS	-1.26	NA	NA	NA	0.04	1	9.31×10^{-01}	NA	NA
6	84076544	A	T	rs1781747	ME1	AAV GWAS	0.35	NA	NA	NA	0.32	1.07	6.83×10^{-01}	NA	NA
8	56953415	G	T	rs182832	LYN	external candidate	2.17	NA	NA	NA	0.21	0.87	4.30×10^{-02}	NA	NA
11	27186775	C	G	rs1838012	CCDC34;BBOX1	AAV GWAS	0.2	NA	NA	NA	0.06	1.02	7.82×10^{-01}	NA	NA
3	8750379	A	C	rs2072582	CAV3	AAV GWAS	-0.01	NA	NA	NA	0.19	0.92	8.52×10^{-01}	NA	NA
X	85677532	A	G	rs2092227	DACH2	AAV GWAS	NA	0.05	0.41	7.75×10^{-07}	0	NA	NA	NA	NA
19	61119102	A	C	rs2163826	NLRP13	AAV GWAS	-1.13	NA	NA	NA	0.16	1.18	1.43×10^{-01}	NA	NA
16	24115989	C	T	rs2283549	PRKCB	external candidate	-1.52	NA	NA	NA	0.21	0.82	1.39×10^{-01}	NA	NA
8	24706384	C	T	rs2607613	ADAM7;NEFM	AAV GWAS	-1.13	NA	NA	NA	0.15	0.77	1.01×10^{-01}	NA	NA
22	21199548	T	C	rs362011	Caucasian SNP	Private Caucasian SNP	0.68	NA	NA	NA	0.32	0.95	4.52×10^{-01}	NA	NA
1	179164192	C	T	rs3747958	NA	Private Caucasian SNP	-0.53	NA	NA	NA	0.4	0.93	3.48×10^{-01}	NA	NA
10	6154666	C	A	rs41295061	IL2RA	external candidate	-0.76	NA	NA	NA	0.08	0.91	2.76×10^{-01}	NA	NA
13	100882487	C	T	rs4586289	NALCN;ITGBL1	AAV GWAS	-0.99	NA	NA	NA	0.15	1.08	3.57×10^{-01}	NA	NA
20	10581313	C	T	rs6040055	JAG1	external candidate	1	NA	NA	NA	0.39	0.95	5.94×10^{-01}	NA	NA

19	791448	A	G	rs62132295	PRTN3	external candidate	0.9	NA	NA	NA	0.33	0.78	$7.14x10^{-05}$	NA	NA
2	69090019	C	T	rs6743513	ANTXR1;GKN1	AAV GWAS	-2.32	NA	NA	NA	0.05	0.94	$5.87x10^{-01}$	NA	NA
22	25019635	C	T	rs688034	SEZ6L	external candidate	0.6	NA	NA	NA	0.34	1.08	$2.29x10^{-01}$	NA	NA
10	49368538	C	G	rs7091343	ARHGAP22	AAV GWAS	NA	NA	NA	NA	0	NA	NA	NA	NA
8	23798666	A	T	rs819196	STC1	external candidate	0.68	NA	NA	NA	0.47	0.88	$4.41x10^{-01}$	NA	NA
6	66294139	A	G	rs9345645	EGFL11	AAV GWAS	1.16	NA	NA	NA	0.2	1.03	$5.99x10^{-01}$	NA	NA
13	40883575	A	C	rs9532806	NARG1L	AAV GWAS	0.11	NA	NA	NA	0.14	1.02	$4.11x10^{-01}$	NA	NA
4	62503784	A	T	rs989295	LPHN3	AAV GWAS	0.02	NA	NA	NA	0.06	1.11	$2.04x10^{-01}$	NA	NA
17	42507913	A	C	rs9908463	CDC27;LOC652203	AAV GWAS	1.18	NA	NA	NA	0.1	1.08	$8.25x10^{-01}$	NA	NA

MAF, minor allele frequency;

OR,odds ratio;

[a]Cochran-Armitage trend test.

Chr,chromosome.

P, P value for the Cochran-Armitage statistic

Table S7. Stepwise conditional analysis of association in the HLA region in the primary cohort

Test SNP	Conditioning SNP(s)	Unconditioned P[1]	Conditioned P[2]	HLA locus
rs3117242	rs3117242	$2.67x10^{-48}$	NA	HLA-DPB1;HLA-DPB2
rs3129248		$4.47x10^{-8}$	0.004	COL11A2;HLA-DPB2
rs3117016		$2.84x10^{-13}$	0.016	HLA-DPB2
rs3130233		$2.08x10^{-8}$	0.029	HLA-DPB2
rs7744381		$7.06x10^{-14}$	0.117	HLA-DPB2
rs3128966		$1.28x10^{-26}$	0.437	HLA-DPB1;HLA-DPB2
rs3117242	rs3117242	$2.67x10^{-48}$	NA	HLA-DPB1;HLA-DPB2
rs3129248	rs3129248	$4.47x10^{-8}$	NA	COL11A2;HLA-DPB2
rs3117016		$2.84x10^{-13}$	0.001	HLA-DPB2
rs3130233		$2.08x10^{-8}$	0.030	HLA-DPB2
rs7744381		$7.06x10^{-14}$	0.034	HLA-DPB2
rs3128966		$1.28x10^{-26}$	0.175	HLA-DPB1;HLA-DPB2
rs3117242	rs3117242	$2.67x10^{-48}$	NA	HLA-DPB1;HLA-DPB2
rs3129248	rs3129248	$4.47x10^{-8}$	NA	COL11A2;HLA-DPB2
rs3117016	rs3117016	$2.84x10^{-13}$	NA	HLA-DPB2
rs3130233		$2.08x10^{-8}$	0.161	HLA-DPB2
rs7744381		$7.06x10^{-14}$	0.001	HLA-DPB2
rs3128966		$1.28x10^{-26}$	0.007	HLA-DPB1;HLA-DPB2
rs3117242	rs3117242	$2.67x10^{-48}$	NA	HLA-DPB1;HLA-DPB2
rs3129248	rs3129248	$4.47x10^{-8}$	NA	COL11A2;HLA-DPB2
rs3117016	rs3117016	$2.84x10^{-13}$	NA	HLA-DPB2
rs3130233		$2.08x10^{-8}$	0.095	HLA-DPB2
rs7744381	rs7744381	$7.06x10^{-14}$	NA	HLA-DPB2
rs3128966		$1.28x10^{-26}$	0.204	HLA-DPB1;HLA-DPB2
rs3117242	rs3117242	$2.67x10^{-48}$	NA	HLA-DPB1;HLA-DPB2
rs3129248	rs3129248	$4.47x10^{-8}$	NA	COL11A2;HLA-DPB2
rs3117016	rs3117016	$2.84x10^{-13}$	NA	HLA-DPB2
rs3130233	rs3130233	$2.08x10^{-8}$	NA	HLA-DPB2
rs7744381	rs7744381	$7.06x10^{-14}$	NA	HLA-DPB2
rs3128966		$1.28x10^{-26}$	0.179	HLA-DPB1;HLA-DPB2

[1]Unconditioned P: The P-value for association of the test SNP with disease in a logistic regression (LR) model including only this SNP alongside the subjects' geographic regions as a stratifying variable.

[2]Conditioned P: The P-value for association in a similarly constructed LR model in which the conditioning SNP is accounted for prior to adding the test SNP.

Table S8: Subset analysis by ANCA immunofluorescence

SNP	Chr	Overall analysis 2267 v 6858		ANCA immunofluorescence: cANCA v pANCA 1646 v 648		cANCA v control		pANCA v control	
		OR	P	OR	P	OR	P	OR	P
rs3117242 HLA-DP	6	3.67	$1.5x10^{-71}$	5.08	$2.46x10^{-47}$	7.02	$5.66x10^{-94}$	1.51	$2.02x10^{-2}$
rs3130233 COL11A2	6	1.51	$7.8x10^{-15}$	1.80	$6.76x10^{-14}$	1.71	$2.66x10^{-24}$	0.90	$6.92x10^{-1}$
rs3117016 COL11A2	6	1.83	$6.4x10^{-24}$	2.45	$6.89x10^{-30}$	2.35	$2.13x10^{-42}$	NA	$2.36x10^{-1}$
rs5000634 HLA-DQA1	6	0.80	$2.9x10^{-09}$	1.31	$2.38x10^{-3}$	0.85	$1.17x10^{-4}$	0.64	$4.22x10^{-9}$
rs1705767 ARHGAP18	6	0.80	$6.2x10^{-07}$	0.85	$5.20x10^{-1}$	0.78	$3.90x10^{-7}$	0.90	$6.36x10^{-2}$
rs7151526 SERPINA1	14	0.59	$2.4x10^{-09}$	0.66	$2.06x10^{-2}$	0.51	$4.44x10^{-11}$	0.82	$1.90x10^{-1}$
rs62132295 PRTN3	19	0.83	$6.6x10^{-04}$	0.74	$8.98x10^{-4}$	0.77	$1.31x10^{-5}$	1.06	$4.54x10^{-1}$
rs6628825 MOSPD2	X	0.79	$9.7x10^{-06}$	0.78	$8.04x10^{-2}$	0.76	$2.20x10^{-7}$	0.88	$4.08x10^{-1}$

Chr, chromosome
OR, Odds ratio
P, p value for Cochran-Armitage trend test

Table S9. MHC associations with GPA, MPA, PR3 and MPO in an Italian cohort															
				Italian MPA cohort (82 cases, 449 controls)			Italian GPA cohort (115 cases,449 controls)			Italian MPO cohort (80 cases, 449 controls)			Italian PR3 cohort		
SNP	Locus	OR*	MAF*	Power	OR	p	Power	OR	p	Power	OR	p	Power	OR	p
rs3117242	HLA-DP	3.67	0.21	1	1.1	0.71	1	5.2	1.7×10^{-11}	1	1.1	0.67	1	9.8	7.87×10^{-12}
rs5000634	HLA-DQ	0.67	0.39	0.39	0.5	4.0×10^{-4}	0.53	0.9	0.60	0.39	0.5	1.46×10^{-3}	0.41	0.8	0.27

* derived from primary and replication cohort data

Table S10. Haplotype analysis of the *SERPINA1* Z allele SNP (rs28929474) and rs7151526

SNP		Discovery cohort			Replication cohort		
rs7151526	rs28929474	Freq. controls	Freq. cases	OR (95% CI)	Freq. controls	Freq. cases	OR (95% CI)
A	A	0.0002	0.0439	12.02 (4.05-35.72)	0.0089	0.0374	4.14 (2.61-6.58)
A	G	0.0430	0.0311	0.82 (0.58-1.14)	0.0364	0.0311	0.88 (0.67-1.16)
C	A	0.0233	0.0018	0.08 (0.02-0.34)	0.0039	0.0039	0.85 (0.34-2.14)
C	G	0.9334	0.9232	1 (reference)	0.9508	0.9276	1 (reference)

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